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# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 1 of 1

<b>Application Number</b>	10/008,982
<b>Filing Date</b>	12/06/2001
<b>First Named Inventor</b>	KUO, et al
<b>Group Art Unit</b>	484 1624
<b>Examiner Name</b>	COLEMAN
<b>Attorney Docket Number</b>	ORT-1551

## U.S. PATENT DOCUMENTS

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## FOREIGN PATENT DOCUMENTS

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Examiner Signature	Brenda Coleman	Date Considered	Sept. 29, 2003
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Substitute for form 1449A/PTO

<b>Application Number</b>	10/008,982
<b>Filing Date</b>	12/06/2001
<b>First Named Inventor</b>	KUO, et. al.
<b>Group Art Unit</b>	1614-1624
<b>Examiner Name</b>	COLEMAN
<b>Attorney Docket Number</b>	ORT-1551

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Sheet 1 of 8

U.S. PATENT DOCUMENTS

or relevant figures appear	
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## FOREIGN PATENT DOCUMENTS

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Examiner Signature	Brenda Coleman	Date Considered	Sept. 29, 2003
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# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 2 of 8

Application Number	10/008,982
Filing Date	12/06/2001
First Named Inventor	KUO, et. al.
Group Art Unit	1614 1624
Examiner Name	COLEMAN
Attorney Docket Number	ORT-1551

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OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITOL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
BC	1	AHMAD, S., et al., "Expression of the Antisense cDNA for Protein Kinase C $\alpha$ Attenuates Resistance in Doxorubicin-Resistant MCF-7 Breast Carcinoma Cells," <i>Molecular Pharmacology</i> , 1993, 43:858-862	
BC	2	AKINAGAKA, S., et al., "Antitumor Activity of UCN-01, a Selective Inhibitor of Protein Kinase C, in Murine and Human Tumor Models," <i>Cancer Res.</i> , 1991, 51: 4888-4892	
BC	3	BASTYR III, E. J. and LU, J., "Increased Platelet Protein Kinase C- $\beta$ (PKC- $\beta$ ) in IDDM," <i>Diabetes</i> , 1993, 42, (Suppl. 1) 97A	
BC	4	BEGEMANN, M., et al., "Treatment of Human Glioblastoma Cells with the Staurosporine Derivative CGP 41251 Inhibits CDC2 and CDK2 Kinase Activity and Increases Radiation Sensitivity," <i>Anticancer Res. (Greece)</i> , 1998, 4A, 18:2275-2282	
BC	5	BELDHUIS, H.J.A., et al., "Long-Term Increase in protein Kinase C- $\gamma$ and Muscarinic acetylcholine Receptor expression in the Cerebral Cortex of Amygdala-Kindled Rats-A Quantitative Immunocytochemical Study," <i>Neuroscience</i> , 1993, 55:965-73	
BC	6	BENDER, S. L. and GAUTHIER, D. R., "an Approach to Pancreatistatin from myo-Inositol", <i>Tetrahedron Lett.</i> , 1996, 37:13-16	
BC	7	BERGER, J., and HAYES, N. S., "A High-Capacity Assay for Activators of Glucose Incorporation into Glycogen in L6 Muscle Cells," <i>Anal. Biochem.</i> , 1998, 261: 159-163	
BC	8	BILDER, G. E., et al., "Phorbol-12, 13-Dibutyrate-Induced Vasoconstriction in Vivo: Characterization of Response in Genetic Hypertension," <i>J. Pharmacol. Exp. Ther.</i> , 1990, 252:526-530	
BC	9	BOLLAG, W. B., et al., "Effects of the selective Protein Kinase C Inhibitor, Ro 31-7549, on the Proliferation of cultured Mouse Epidermal Keratinocytes," <i>J. Invest. Dermatol.</i> , 1993, 100:240-246	
BC	10	CHEN, Y. H., et al., "Sequence of the Human Glycogen-Associated Regulatory Subunit of Type 1 Protein Phosphatase and Analysis of Its Coding Region and mRNA Level in Muscle From Patients With NIDDM," <i>Diabetes</i> , 1994, 43:1234-1241	
BC	11	CHEN, K. S., et al., "Diacylglycerol-Protein Kinase C Signalling In Skeletal Muscle: A Possible Link To Insulin Resistance," <i>Trans. Assoc. Am. Physicians</i> , 1991, 104:206-212;	
BC	12	CHIN, J. E., et al., "Overexpression of Protein Kinase C Isoenzymes $\alpha$ , $\beta$ I, $\gamma$ , and $\epsilon$ in Cells Overexpressing the Insulin Receptor," <i>J. Biol. Chem.</i> , 1993, 268: 6338-6347	
BC	13	COHEN P., "Dissection of the Protein Phosphorylation Cascades Involved in Insulin and Growth Factor Action," <i>Biochem. Soc. Trans.</i> , 1993, 21:555-567	
BC	14	COTTER D., et al. "Abnormalities of Wnt signalling in schizophrenia - evidence for neurodevelopmental abnormality," <i>Neuroreport</i> , 1998, 9:1379-1383;	
BC	15	CRAVEN, P. A. and Derubertis, F. R., "Protein Kinase C is Activated in Glomeruli from streptozotocin Diabetic Rats," <i>J. Clin. Invest.</i> , 1989, 83:1667-1675;	

Examiner Signature	Brenda Coleman	Date Considered	Sept. 29, 2003
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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

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Sheet 3 of 8

Application Number	10/008,982
Filing Date	12/06/2001
First Named Inventor	KUO, et al.
Group Art Unit	1614
Examiner Name	COLEMAN
Attorney Docket Number	ORT-1580

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Examiner's Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITOL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
BC	16	CROSS, D. A. E., et al., "The Inhibition of glycogen synthase kinase-3 by insulin or insulin-like growth factor 1 in the rat skeletal muscle cell line L6 is blocked by wortmannin, but not by rapamycin: evidence that wortmannin blocks activation of the mitogen-activated protein kinase pathway in L6 cells between Ras and Raf", <i>Biochemical Journal</i> , 1994, 303:21-26	
BC	17	DANSO, D., et al., "The protein kinase C (PKC) inhibitor Ro32-0432 (Ro) significantly enhances mitomycin-C (MMC) induced apoptosis", <i>Proc. Am. Assoc. Cancer Res.</i> , 1997, 38:92	
BC	18	DEKKER, L. V., et al., "Protein Kinase C- $\beta$ contributes to NADPH oxidase activation in neutrophils", <i>Biochem. J.</i> , 2000, 347:285-289	
BC	19	D'MELLO, S. R., et al., "Lithium induces Apoptosis in Immature Cerebellar Granule Cells but Promotes Survival of Mature Neurons", <i>Exp. Cell Res.</i> , 1994, 211:332-338	
BC	20	EASTMAN, Q., et al., "Regulation of LEF-1/TCF Transcription factors by Wnt and other signals," <i>Current Opinion in Cell Biology</i> , 1999, 11:233-240	
BC	21	ELDAR-FINKELMAN, H., et al., "Increased Glycogen Synthase Kinase-3 Activity in Diabetes-and Obesity-Prone C57BL/6J Mice", <i>Diabetes</i> , 1999, 48:1-5	
BC	22	ELDAR-FINKELMAN, H., et al., "Expression and characterization of glycogen synthase kinase-3 mutants and their effect on glycogen synthase activity in intact cells", <i>PNAS</i> , 1996, 93:10228-10233	
BC	23	ELDAR-FINKELMAN, H., and Krebs, E. G., "Phosphorylation of insulin receptor substrate 1 by glycogen synthase kinase 3 impairs insulin action", <i>PNAS</i> , 1997, 94:9660-9664	
BC	24	EMBI, N., et al., "Glycogen Synthase Kinase-3 from Rabbit Skeletal Muscle", <i>Eur. J. Biochem.</i> , 1980, 107:519-527	
BC	25	FAUL, M. M., et al., "A General Approach to the Synthesis of Bisindolylmaleimides: Synthesis of Staurosporine Aglycone", <i>Synthesis</i> , 1995, 1511-1516	
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BC	27	GAT, U., et al., "De Novo Hair Follicle Morphogenesis and Hair Tumors in Mice Expressing a Truncated $\beta$ -Catenin in Skin," <i>Cell</i> , 1998, 95:605-614	
BC	28	GOULD, P. L., "Salt selection for basic drugs", <i>International J. Pharm.</i> , 1986, 33:201-217	
BC	29	GU, X., et al., "Increased Protein Kinase C and Isozyme Redistribution in Pressure-Overload Cardiac Hypertrophy in the Rat", <i>Circ. Res.</i> , 1994, 75:926-931	
BC	30	HANCOCK, B. C., et al., "Characteristics and significance of the Amorphous State in Pharmaceutical Systems", <i>Journal of Pharmaceutical Sciences</i> , 1997 86:1-12	
BC	31	HARA, H., et al., "Staurosporine, a Novel Protein Kinase C Inhibitor Prevents Postischemic Neuronal Damage in the Gerbil and Rat", <i>J. Cereb. Blood Flow Metab.</i> , 1990, 10:646-653	
BC	32	HARRINGTON, E.O., et al., "Enhancement of Migration by Protein Kinase C $\alpha$ and Inhibition of Proliferation and Cell Cycle Progression by Protein Kinase C $\delta$ in Capillary Endothelial Cells", <i>J. Biol. Chem.</i> , 1997, 272:7390-7397	

Examiner  
Signature

Brenda Coleman

Date  
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Sept. 29, 2003

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# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 4 of 3

Application Number	10/008.982
Filing Date	12/6/2001
First Named Inventor	KUO, et al
Group Art Unit	1814 1624
Examiner Name	COLEMAN
Attorney Docket Number	ORT-1551

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OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITOL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
BC	33	HEGEMANN, L., et al., "Effects of tflucarbine as a dual protein kinase C/calmodulin antagonist on proliferation of human keratinocytes and release of reactive oxygen species from human leukocytes", <i>Arch. Dermatol. Res.</i> , 1991, 283:456-460	
BC	34	HOEFLICH, K. P., et al., "Requirement for glycogen synthase kinase-3 $\beta$ in cell survival and NF- $\kappa$ B activation", <i>Nature</i> , 2000, 406:86-90	
BC	35	HONG, M., et al., "Lithium Reduces Tau Phosphorylation by Inhibition of Glycogen Synthase Kinase-3", <i>J. Biol. Chem.</i> , 1997, 272:25326-32	
BC	36	HORN, F., et al., "Decreased Protein Kinase C Activity in Psoriatic Versus Normal Epidermis," <i>J. Invest. Dermatol.</i> , 1987, 88:220-222	
BC	37	HSIEH, J., et al., "Human vitamin D receptor is selectively phosphorylated by protein kinase C on serine 51, a residue crucial to its trans-activation function", <i>Proc. Natl. Acad. Sci. USA</i> , 1991, 88:9315-9319	
BC	38	HSIEH, J., et al., "Phosphorylation of the Human Vitamin D Receptor by Protein Kinase C", <i>J. Biol. Chem.</i> , 1993, 268:15118-15126	
BC	39	HUANG, K. P., "The mechanism of protein kinase C activation," <i>Trends Neurosci.</i> , 1989, 12:425-432	
BC	40	IKEDA, S., et al., "Axin, a negative regulator of the Wnt signaling pathway, forms a complex with GSK-3 $\beta$ -dependent phosphorylation of $\beta$ -catenin," <i>EMBO J.</i> , 1998, 17:1371-1384	
BC	41	INOUCHI, T., et al., "Preferential elevation of protein kinase C isoform $\beta$ II and diacylglycerol levels in the aorta and heart of diabetic rats: Differential reversibility to glycemic control by islet cell transplantation," <i>Proc. Natl. Acad. Sci. USA</i> , 1992, 89:11059-11065	
BC	42	ISHII, H., et al., "Amelioration of Vascular Dysfunctions in Diabetic Rats by an Oral PKC $\beta$ Inhibitor", <i>Science</i> , 1996, 272:728-731	
BC	43	ISHII, H., et al., "Protein kinase C activation and its role in the development of vascular complications in diabetes mellitus," <i>J. Mol. Med.</i> , 1998, 76:21-31	
BC	44	KARASIK, A., et al., "Increased Protein Kinase C Activity Is Linked to Reduced Insulin Receptor Autophosphorylation in Liver of Starved Rats," <i>J. Biol. Chem.</i> , 1990, 265:10226-10231	
BC	45	KELLY, T. A., et al., "Novel Non-Nucleoside Inhibitors of Human Immunodeficiency Virus Type 1 Reverse Transcriptase. 6. 2-Indol-3-yl-and 2-Azaindol-3-yl dipyrrodozepinones(1)," <i>J. Med Chem.</i> 1997, 40: 2430-2433	
BC	46	KOBAYASHI, I., et al., "Platelet-activating factor modulates microvascular transport by stimulation of protein kinase C," <i>Amer. Phys. Soc.</i> , 1994, H1214-H1220	
BC	47	KONIG, A., et al., "The protein kinase C inhibitor RO 32-0432 enhances fludarabine-induced apoptosis in WSU-CLL chronic lymphocytic leukemia cells," <i>Blood</i> , 1997, 90, 10, Suppl. 1 Pt. 2).	

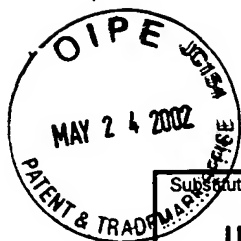
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# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 5 of 8

Application Number	10/008,982
Filing Date	12/6/2001
First Named Inventor	KUO et al
Group Art Unit	4644 1624
Examiner Name	COLEMAN
Attorney Docket Number	ORT-1551

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## OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner's Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITOL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
BC	48	LEE, T-S., et al., "Differential Regulation of Protein Kinase C and (Na,K)-Adenosine Triphosphatase Activities by Elevated Glucose Levels in Retinal Capillary Endothelial Cells," <i>J. Clin. Invest.</i> , 1989, 83:90-94	
BC	49	LEE, T-S., et al., "Activation of protein kinase C by elevation of glucose concentration: Proposal for a mechanism in the development of diabetic vascular complications," <i>Proc. Natl. Acad. Sci. USA</i> , 1989, 86:5141-5145	
BC	50	LEITGES, M., et al., "Immunodeficiency in Protein Kinase C $\beta$ -Deficient Mice," <i>Science</i> , 1996, 273:788-789	
BC	51	LIJAM N., et al., "Social Interaction and Sensorimotor Gating Abnormalities in Mice Lacking <i>Dvll</i> ", <i>Cell</i> , 1997, 90:895-905	
BC	52	MAGEE, D. I AND BECK, E. J., "The use of the Ramberg-Backlund rearrangement for the formation of aza-macrocycles: a total synthesis of manzamine C," <i>Can. J. Chem.</i> , 2000, 78:1060-1066	
BC	53	MALMBERG, A. B., et. al., "Preserved Acute Pain and Reduced Neuropathic Pain in Mice Lacking PKC $\gamma$ ," <i>Science</i> 1997, 278:279-283	
BC	54	MANJI, H. K., et al., "Modulation of CNS Signal Transduction Pathways and Gene Expression by Mood-Stabilizing Agents: Therapeutic Implications," <i>J. Clin. Psychiatry</i> , 1999, 60:27-39 (suppl 2 for review)	
BC	55	MATSUMOTO, H. and SASAKI, Y., "Staurosporine, A Protein Kinase C Inhibitor Interferes With Proliferation of Arterial Smooth Muscle Cells," <i>Biochem. Biophys. Res. Commun.</i> , 1989, 158:105-109	
BC	56	MEYER, T., et al., "A Derivative of Staurosporine (CGP 41 251) Shows Selectivity For Protein Kinase C Inhibition and In Vitro Anti-Proliferative As Well As In Vivo Anti-Tumor Activity," <i>Int. J. Cancer</i> , 1989, 43:851-856	
BC	57	MILETIC, V., et al., "Loose ligation of the rat sciatic nerve is accompanied by changes in the subcellular content of protein kinase C beta II and gama in the spinal dorsal horn," <i>Neurosci. Lett.</i> , 2000, 288:199-202	
BC	58	MUID, R. E., et al., "A novel conformationally restricted protein kinase C inhibitor, Ro 31-8425, inhibits human neutrophil superoxide generation by soluble, particulate and post-receptor stimuli," <i>FEBS Lett.</i> , 1990, 293:169-172	
BC	59	MULQUEEN, M. J., et al., "Oral, anti-inflammatory activity of a potent, selective, protein kinase C inhibitor," <i>Agents Actions</i> , 1992, 37:85-89	
BC	60	MURRAY, N. R., et al., "Protein Kinase C Isotypes in Human Erythroleukemia (K562) Cell Proliferation and Differentiation," <i>J. Biol. Chem.</i> , 1993, 268:15847-15853	
BC	61	NAGPALA, P.G., et al., "Protein Kinase C $\beta$ (1) Overexpression Augments Phorbol Ester-Induced Increase in Endothelial Permeability," <i>J. Cell Physiol.</i> , 1996, 166:249-55	
BC	62	NECHUSHTAN, H., et al., "Inhibition of degranulation and interleukin-6 production in mast cells derived from mice deficient in protein kinase C $\beta$ ," <i>Blood</i> , 2000 (March), 95(5):1752-1757	

Examiner Signature	Brenda Coleman	Date Considered	Sept. 29, 2003
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Sheet 6 of 8

Application Number	10/008,982
Filing Date	12/6/2001
First Named Inventor	KUO et al
Group Art Unit	1614 1624
Examiner Name	COLEMAN
Attorney Docket Number	ORT-1551

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OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITOL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
BC	63	NONAKA, S. and CHUANG, D-M., "Neuroprotective effects of chronic lithium n focal cerebral ischemia in rats," <i>NEUROREPORT</i> , 1998, 9(9):2081-2084	
BC	64	PAP, M. and COOPER, G. M., "Role of Glycogen Synthase Kinase-3 in the Phosphatidylinositol 3-Kinase/Akt Cell Survival Pathway," <i>J. Biol. Chem.</i> , 1998, 273:19929-19932	
BC	65	PARKER P.J., et al., "Glycogen Synthase from Rabbit Skeletal Muscle; Effect of Insulin on the State of Phosphorylation of the Seven Phosphoserine Residues in vivo," <i>Eur. J. Biochem.</i> , 1983, 130:227-234,	
BC	66	RABBI, M.F., et al., "The cAMP-Dependent Protein Kinase A and Protein Kinase C-β Pathways Synergistically Interact to Activate HIV-1 Transcription in Latently Infected Cells of Monocyte/Macrophage Lineage," <i>Virology</i> , 1998, 245(2):257-69	
BC	67	RAYNAUD, F. and EVAIN-BRION, D., "Protein kinase C activity in normal and psoriatic cells: cultures of fibroblasts and lymphocytes," <i>Br. J. Dermatol.</i> , 1991, 124:542-546	
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